

REMARKS

Claims 1-6, 12-17, 56-57 and 69-78 were pending. Applicants have amended claim 78 to improve its form, and have canceled claims 1-6, 12-17, 57 and 77, without prejudice, to clarify the claimed subject matter. These amendments do not introduce any new matter. Applicants request entry of these amendments such that claims 56, 69-76 and 78 will be pending.

Claim Objections

The Examiner objects to claim 78 for informalities, contending that it appears the claim should read "A packaged pharmaceutical comprising..." Applicants have amended the claim as requested, thereby obviating this ground of rejection.

Information Disclosure Statement

The Examiner objects to the document listed as U.S. Patent No. 5,733,441 (Higley et al.), contending that the Patent No. refers to a document by Chi Yin-Ko pertaining to a pre-wet filter system. The Examiner suggests that this is a typing error on the IDS form.

Applicants submit with this Response a Supplemental Information Disclosure Statement with the corrected document listing, thereby obviating this ground of objection.

Claim Rejections – 35 USC § 103

Claims 56, 70-76 and 78 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Sampath et al. ("Sampath") in view of London et al. ("London"). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the pharmaceutical containing an OP/BMP morphogen, as allegedly taught by Sampath, by

formulating a pharmaceutical further encompassing an ACE inhibitor, as allegedly taught by London.

Further, claims 56 and 69 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Sampath in view of London as applied to claims 56, 70-76 and 78 in the preceding paragraphs and further in view of Salvetti ("Salvetti"). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a pharmaceutical comprising an OP/BMP morphogen, as allegedly referred to by Salvetti, and further comprising an ACE inhibitor, as allegedly referred to by London, said ACE inhibitor being enalapril, as allegedly referred to by Salvetti.

Pursuant to MPEP 716.02(a)(II), "[e]vidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness." *See also In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987): "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties... can be enough to rebut a *prima facie* case of obviousness."

Applicants have disclosed unexpectedly superior properties in the claimed compositions over a spectrum of properties. This is sufficient to rebut the alleged *prima facie* case of obviousness.

For example, the specification teaches that the combination of OP-1 and enalapril is far superior in treating proteinuria than either component alone: "OP-1 (10 or 30 µg/kg) or enalapril reduced the proteinuria level, from about 180 mg/dL/24 hr to about 80 (or 110) or 140 mg/dL/24 hr, respectively. In contrast, the combination of OP-1 and enalapril [sic] dramatically [sic] reduced the proteinuria level to as low as about 30 mg/dL/24 hr (P<0.01)." (*See* page 143, lines 6-10.) The

specification further states that "[t]he combination of OP-1 and enalapril was more effective in reducing the proteinuria level than enalapril alone, 62 mg/day vs. 105 mg/day." (See page 139, lines 14-16.)

Additionally, the specification discloses an unexpected synergy between OP-1 and enalapril in improving the Glomerular Filtration Rate (GFR). While enalapril has no significant effect on its own in improving GFR, applicants have found that enalapril is able to improve GFR in the presence of OP-1:

"OP-1, but not enalapril, significantly increased the glomerular filtration rate (GFR). While the mean GFR in the 32-week diabetic animals was about 0.38 ml/min/100 g body weight, the mean GFR in the animals treated with 100 µg/kg of OP-1 was about 0.7 ml/min/100 g body weight (P<0.05). The mean GFR in the animals co-treated with OP-1 and enalapril was even higher, about 0.75 ml/min/100 g body weight (P<0/05)." (See page 142, lines 5-10.)

In sum, the combination of the OP/BMP morphogen and the ACE inhibitor exhibit at least two unexpected advantageous properties: superior treatment of proteinuria and superior increase in GFR as compared to the morphogen alone or the ACE inhibitor alone. These unexpected properties of the claimed combination are sufficient to rebut a *prima facie* case of obviousness. Applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Obviousness-Type Double Patenting

Claims 56, 71-76 and 78 stand rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being obvious over claims 1-13 of U.S. Patent No. 6,677,432 ('432) or claims 1-5 of U.S. Patent No. 6,846,906 ('906). The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a

pharmaceutical comprising an OP/BMP morphogen, as allegedly referred to by '432 or '906, for the treatment of renal failure, as allegedly referred to by Vukicevic, and further comprising an ACE inhibitor, as allegedly referred to by London.

Further, claims 56 and 69 stand rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being obvious over claims 1-13 of U.S. Patent No. 6,677,432 ('432) or claims 1-5 of U.S. Patent No. 6,846,906 ('906) in view of London as applied to claims 56, 71-76 and 78 in the preceding paragraphs and further in view of Vukicevic and Salveti. The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify a pharmaceutical comprising an OP/BMP morphogen, as allegedly referred to by '432 or '906, for the treatment of renal failure, as allegedly referred to by Vukicevic, to further encompass an ACE inhibitor, as allegedly referred to by London, said ACE inhibitor being enalapril, as allegedly referred to by Salveti.

In response, Applicants will consider filing a suitable disclaimer upon notification of allowable subject matter.

The Office Action provisionally rejects claims 56, 69, 71-76 and 78, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over co-pending Application No. 10/816,768. In response, Applicants submit that, pursuant to MPEP 804, "[i]f the 'provisional' double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the 'provisional' double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." Therefore, Applicants are not required to amend the claims at this time.


CONCLUSIONS

In view of the above amendments, Applicants believe the pending application is in condition for allowance.

Applicants believe no additional fee is due with this response beyond those listed in the fee transmittal sheet. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P01-599 from which the undersigned is authorized to draw.

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Respectfully submitted,

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